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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/700,879	11/20/2000	Tatsuya Tamura	TAMURA-5	4195

1444 7590 01/26/2005

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EXAMINER	
MAIER, LEIGH C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/700,879	TAMURA ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-12,17,18 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-12,17,18 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 1, 2004 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Any rejection or objection not expressly repeated has been withdrawn.

Claim Rejections - 35 USC § 103

Claims 1, 5, 8, 12, 23, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over AKIMA et al (US 5,733,891).

The claims are drawn to a conjugate of at least one therapeutic agent for joint disease which is bonded via a spacer to hyaluronic acid (HA) or derivative, wherein the spacer is attached to a carboxylic moiety of the HA to form an amide bond. Dependents are drawn to the amount of therapeutic agent present in the conjugate, the type of spacer, and a pharmaceutical composition comprising said conjugate.

AKIMA teaches the preparation of HA conjugates wherein a therapeutic agent is attached to the HA via an amide bond. See col 2, lines 15-19. The reference exemplifies daunomycin attached by means of an ε–aminocaproic acid spacer, wherein the spacer-HA bond forms an

amide. The reference further teaches a drug content of about 0.1 to 30 wt%. See example 2. The reference does not exemplify a conjugate comprising a therapeutic agent for joint disease. However, the reference expressly suggests the use of other agents, such as prednisolone, an agent that Applicant admits has utility for the treatment of joint disease. See col 3, line 12 of reference and page 16, section (4) of specification.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the exemplified HA conjugate by the substitution of any of the suggested therapeutic agents, such as prednisolone and a pharmaceutical composition thereof, for the art disclosed utility with a reasonable expectation of success. It would be within the scope of the artisan to optimize the amount of the therapeutic agent within the range taught in the reference. This range is fully encompassed by the range recited in claim 5.

Claims 1, 3, 5-10, 12, 18, 23, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over AKIMA et al (US 5,733,891) and GALLARDY et al (WO 92/09563).

The invention is as set forth above. Claims 3, 6, 7, 9, 10, and 18 limit the therapeutic agent to an MMP inhibitor.

AKIMA teaches as set forth above. The reference teaches drug delivery generally, with an emphasis on the use of anti-cancer agents. The reference does not teach MMP inhibitors.

GALLARDY teaches MMP inhibitors, as discussed in previous Office actions. GALLARDY teaches that the MMP inhibitors have utility for the treatment of such disorders as tumor metastasis and rheumatoid arthritis. See page 10, lines 12-18.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the HA conjugates taught by AKIMA by substituting any anti-cancer agent, such as an MMP inhibitor with a reasonable expectation of success. The artisan would be motivated to prepare such a conjugate or pharmaceutical composition thereof for the art disclosed utility of cancer treatment.

Claims 1, 3, 5-12, 17, 18, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over PRESTWICH et al (US 5,874,417) in view of AKIMA et al (US 5,733,891) and GALLARDY et al (WO 92/09563).

The invention is as set forth above. Claims 11,17, 22, and 25 are drawn to methods of using the conjugates described above for the treatment of joint diseases.

As discussed in the previous Office action, PRESTWICH teaches HA conjugates comprising various anti-inflammatories linked via a spacer attached to an HA carboxyl. See examples 2, 3, and 12. These products have utility for the treatment of various forms of arthritis. See col 14, lines 38-45. The reference does not teach conjugates wherein the spacer is attached via an amide bond.

AKIMA and GALLARDY teach as set forth above.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer the HA conjugates taught by AKIMA or the combination of AKIMA and GALLARDY for the treatment of joint diseases, such as various types of arthritis, with a reasonable expectation of success. PRESTWICH had established that HA conjugates of therapeutic agents for joint diseases have that utility. In the absence of unexpected results, one of

ordinary skill would reasonably expect that conjugates having a slightly difference mode of attachment would have the same utility as those taught by PRESTWICH.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 872-9306.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier

Leigh C. Maier
Patent Examiner
January 21, 2005